

## REMARKS

Upon entry of the amendment, claims 2, 3, 5-8, 39-43, and 45-65 are pending in the present application. Support for the amendments is found throughout the specification. No new matter has been added.

### Rejections under 35 U.S.C. § 112, first paragraph

#### *Written Description*

Claims 2, 3, 5-8, and 39-43, and 45-65 are rejected as being inadequately described. In maintaining this rejection, the Office asserts that the specification fails to provide a representative number of polypeptides containing a sequence with at least 95% sequence identity to SEQ ID NO: 2 and having the ability to modulate NF $\kappa$ B signaling pathway.

As amended, claim 2, from which claims 3, 5-8, 39-43, and 45-52 depend, and claim 53, from which claims 54-65 depend, are now directed to methods of modulating NF $\kappa$ B activity by contacting cells with TRADE polypeptides containing the extracellular domain of a TRADE $\alpha$  polypeptide and having the ability to modulate the activity a TRADE $\alpha$  polypeptide. As discussed previously, more than one species of TRADE polypeptides having the claimed features are described in the present disclosure (see Response to Office action mailed March 13, 2005 as well as page 133, lines 8-24 of the specification, Figure 9, and Figure 14A). Exemplary TRADE polypeptides include Flag-TRADE $\alpha$ , Flag-TRADE 1-368, Flag-TRADE 1-328, Flag-TRADE 1-218, and Flag-TRADE 1-196, all of which have the ability to modulate NF $\kappa$ B activity.<sup>1</sup> Thus,

---

<sup>1</sup> As discussed on the November 17, 2005 telephone interview with the Examiner, the ability of TRADE $\alpha$  to modulate NF $\kappa$ B activity is shown in FIGURE 14, where the expression of a full length TRADE $\alpha$  polypeptide stimulates the activity of NF $\kappa$ B relative to such activity in cells expressing an empty vector control. This activity is in turn inhibited by the expression of various fragments of the TRADE $\alpha$  polypeptide.

because a representative number of species for the claimed polypeptides has been provided, Applicants respectfully request that this rejection be withdrawn.

*Enablement*

Claims 2, 3, 5-8, 39-43, and 45-65 are further rejected for lack of enablement. Specifically, the Office states that it is unpredictable whether any polypeptide containing the extracellular domain of TRADE would have the ability to modulate NF $\kappa$ B activity.

As discussed above, the amended claims are now directed to TRADE polypeptides containing the extracellular domain of a TRADE $\alpha$  polypeptide and having the ability to modulate the activity of NF $\kappa$ B. The specification provides multiple examples of polypeptides having such features. Contrary to the Office's assertion, all of the TRADE polypeptides provided in the specification have the ability to either stimulate or inhibit NF $\kappa$ B activity<sup>1</sup>. Thus, based on Applicants' disclosure, one skilled in the art could readily practice the claimed invention without undue experimentation.

Moreover, Applicants' disclosure clearly establishes a nexus between the claimed method, the modulation of NF $\kappa$ B, and the modulation of TRADE. Because Applicants successfully modulated NF $\kappa$ B transcription using various TRADE polypeptides, one skilled in the art reading the specification would immediately understand that modulating the NF $\kappa$ B signaling pathway would merely require contacting a cell with TRADE polypeptides, such as those found in Applicants' disclosure. One skilled in the art would also understand that such polypeptides would be useful for treating and preventing any disease that would benefit from the modulation of TRADE $\alpha$  activity or NK $\kappa$ B signaling. Alternatively, one skilled in the art would understand that, based on the teachings in the specification, such polypeptides would also be

useful for the purpose of identifying agents that modulate TRADE expression or activity. Thus, Applicants have enabled more than one use for the claimed invention.

For the foregoing reasons, the § 112, first paragraph rejection for lack of enablement should be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claim 40 is rejected as being indefinite. As requested by the Office, Applicants have amended claim 40 (and claim 61) to specify that the isotype refers to the Fc portion of the fusion polypeptide. This rejection should be withdrawn.

Applicants submit that the application is in condition for allowance, and such action is respectfully requested.

Applicants have enclosed a petition for extension of time and a check in payment of the required fee. Although no additional charges are believed to be due, the Commissioner is authorized to charge any additional fees that may be due, or to credit any overpayment, to the undersigned's account, Deposit Account No. 50-0311, Ref. No. 22058-569.

Respectfully submitted,

Ivor R. Elrifl, Reg. No. 39,529  
David E. Johnson, Reg. No. 41,874  
Attorneys for Applicants  
c/o MINTZ, LEVIN  
One Financial Center  
Boston, Massachusetts 02111  
Tel: (617) 542-6000

Dated: December 1, 2005

TRA 2097140v.1